continually exposed to the pressure of the shoe. Finally, we may call attention to the small number of colonies. A superficial examination of but a few sections would have failed to reveal the true nature of the disease. Leser had made a similar observation in studying his own cases. In Milian's patient this same difficulty led to the probable diagnosis of tuberculosis. Perhaps a more thorough microscopic study of localized lesions of this type may cause us to change our present views as to the infrequency of actinomycosis of the skin.

HEMORRHAGES IN THE COURSE OF BRIGHT'S DISEASE, WITH ESPECIAL REFERENCE TO THE OCCURRENCE OF A HEMORRHAGIC DIATHESIS OF NEPHRITIC ORIGIN.[1]

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The occurrence of hemorrhage as a complication of Bright's disease has been familiar to clinicians since the days of Richard Bright (1827). But even before Bright, Latour,[2] in 1815, called attention to the coincidence of *epistaxis* and other forms of bleeding with dropsy, while the all-observing Morgagni, at a still earlier date, reported the case of a woman in whom, though she already had the odor of urine on her breath, vomiting of blood and bleeding from the nose proved beneficial. Rayer[3] was among the first to appreciate fully the significance of epistaxis as a symptom of Bright's disease. Naumann[4] cites the case of a young man who died in convulsions after having had repeated attacks of violent nose bleed, in one of which he lost as much as six pounds of blood. The autopsy showed enlarged and inflamed kidneys. While admitting that the hemorrhage in such cases might be purely accidental, Rayer was, nevertheless, of the opinion that it was more probably the result of an alteration of the blood, consequent upon the derangement of the urinary secretion.

The close connection between Bright's disease and *cerebral hemorrhage* was strikingly shown in the classical paper of W. Senhouse Kirk,[5] while ophthalmologists have made us familiar with the frequency of hemorrhage into the eye in the course of nephritis.

These various forms of hemorrhage have been attributed, particularly by Huchard,[6] to vascular degeneration and hypertension;

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[1] Read at a meeting of the Association of American Physicians, Washington, D. C., May 7, 8 and 9, 1907.

[2] Quoted by Launois, Thèse de Paris.

[3] Traité des maladies des reins, i, 605.

[4] Quoted by Rayer.

[5] Medical Times and Gazette, xi, 515.

[6] Bull. et mem. Soc. méd. de hôp. de Paris, 1888, 3 s., v, 287-290.

but the interesting studies of Schoenemann[7] seem to demonstrate that, as far as nose bleed is concerned, these are not necessary factors. He found after death numerous superficial hemorrhages into the mucous membrane of the nose. The number of peripheral capillaries, that is, those near the epithelial surface, was increased; in many cases these capillaries had broken through the basal membrane, the capillary loops having forced their way through the basal epithelial cells. During life the capillary walls, as well as the epithelial covering, rupture, and the blood escapes upon the surface. Schoenemann did not observe these conditions in diseases other than nephritis. They cannot be regarded as the result of ordinary circulatory obstruction; the capillary walls themselves seemed normal in appearance, and the deeper vessels showed no degenerative changes, such as have been described in other parts of the body. Perhaps the changes are due to a circulating substance which penetrates by osmosis into the surrounding structures and weakens them and the capillary walls in such a way that they cannot resist the blood pressure.

That *metrorrhagia* may be a symptom of nephritis is not so well known, although several writers have called attention to it. Among the older authorities who mention it are Grainger Stewart,[8] and Lecorché.[9] Braun[10] reports 2 cases of metrorrhagia. Delbet[11] has recorded the case of a girl who died as the result of a profuse vaginal hemorrhage, in his opinion, dependent upon renal disease. Bonifas,[12] in an intractable case of uterine hemorrhage in a woman, aged fifty-five years, saw an arrest of the hemorrhage under antinephritic treatment. Quite recently, Violet[13] reported 3 cases of profuse metrorrhagia, apparently caused by interstitial nephritis. He points out, as does Cumston,[14] the importance of recognizing the connection between metrorrhagia and nephritis, as otherwise improper treatment may be instituted. Ergot, in the opinion of both writers, is contra-indicated in such cases.

Hemorrhage from the lungs, as a manifestation of renal disease, is rare. Cases are recorded by Hawkins,[15] Fisher,[16] and Duclos,[17] and the subject is mentioned by Dickinson, Fuerbringer,[18] and Senator.[19] In Hawkins' case, the hemoptysis continued for a year and two months, the autopsy showing cirrhosis of the kidneys. According to Duclos the hemoptysis, which is most frequent in old persons, is more often a precursor than an accompaniment of interstitial nephritis, and is due to sclerosis of the pulmonary vessels. The same cause that produces these changes in the vessels of the lungs also acts upon those of the kidneys, and thus brings about interstitial nephritis.

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[7] Arch. f. Laryng. und Rhin., 1901-2, xii, 437.

[8] Bright's Diseases, New York, 1871, 238.

[9] Traité de maladies des reins, 1875, 398.

[10] Quoted by Wieger (Launois, loc. cit.).

[11] Bull. soc. anat. de Paris, 1885, lx, 183-186.

[12] La normandie médicale, 1898, xiv, 102.

[13] Lyon médical, 1904, ciii, 428-438.

[14] Buffalo Medical Journal, 1904-1905, 718.

[15] Trans. Clin. Soc., London, 1891-2, xxv, 237-242.

[16] Bristol Med.-Chir., Jour., 1904, xxii, 234-247.

[17] Rev. gén. de clin. et de therap., 1890, iv, 329; 345.

[18] Die Krankheiten der Harn- und Geschlechts-Organe, Braunschweig, 1904, 132.

[19] Nothnagel's Encyclopedia of Practical Medicine, American edition, Diseases of the Kidneys, etc., 227.

Fisher, in addition to 1 case of hemoptysis, reports 4 cases of *hematemesis* associated with small, white kidneys. In explanation of these hemorrhages, he propounds an ingenious hypothesis, to which I shall refer later. Another case of severe gastric hemorrhage, in a nephritic patient of thirty, is reported by Bonifas.[20]

Hematuria, a common symptom of acute nephritis, or of the acute exacerbation of chronic nephritis, may arise in the absence of acute manifestations, as in the cases reported by Askanazy[21] and Kusumoto,[22] in which the hemorrhage occurred apparently from the engorged veins of the renal pelvis.

An interesting form of nephritic hemorrhage is that into the *ear*, of which Schwartze[23] has reported a case. Haug,[24] in an exhaustive paper upon this subject, collects a number of cases from medical literature, all of them examples of hemorrhage into the structures of the ear in Bright's disease. Alibert, in 1880, devoted a thesis to the subject of otorrhagia in nephritis. Hemorrhage into the tympanic cavity may occur even before other symptoms of nephritis are manifest. It thus has the value of an early or prenephritic symptom.

I should not fail to mention the fact that Dieulafoy[25] believes that auditory disturbances, such as tinnitus, partial or complete deafness, and otitis media are more frequent in the course of Bright's disease than disturbances of the eye. Pissot[26] found among 66 cases of chronic nephritis, 34 suffering from auditory disorders.

In addition to the isolated hemorrhages I have so far described, we meet in Bright's disease, with a true *hemorrhagic diathesis*, 2 cases of which have come under my own observation. In a sense, the term hemorrhagic diathesis is also applicable to those cases of epistaxis, metrorrhagia, etc., in which the hemorrhage is uncontrollable, and in which there is no local lesion to explain the bleeding.

Medical literature contains but few references to the hemorrhagic type of bleeding in its relation to Bright's disease. Avrad[27] saw a well-marked example in a case of scarlatinal nephritis. An incomplete report of a case was made by Imbert-Gourbeyer,[28] in 1856. Levi[29] reports 2 cases—1 of parenchymatous nephritis with epistaxis and hemoptysis, terminating in recovery; and 1 of contracted kidney, with dropsy, hemoptysis, and epistaxis, ending in death.

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[20] Loc. cit.

[21] Zeit. f. klin. Med., Band lviii, 432.

[22] Deut. Archiv f. klin. Med., 1907, Band lxxxix, Heft 5 und 6, 405.

[23] Arch. f. Ohrenheilk, iv, 13.

[24] Deutsche med. Wochenschrift, 1896, 723.

[25] La France méd., 1877.

[26] Thèse de Paris, 1878.

[27] Gazette médicale, 1853.

[28] Quoted by Launois.

[29] Quoted by Launois.

Among systematic writers, Senator,[30] Fuerbringer,[31] Castaigne,[32] and Osler[33] mention hemorrhagic diathesis as a rare complication of nephritis. According to Wagner,[34] and to Senator,[35] the hemorrhagic diathesis sometimes precedes and is the cause of nephritis. More probably, however, the cause of the one is the cause of the other. A case of this nature is the one reported by George Johnson.[36] A man, aged thirty-seven years, was seized with epileptiform attacks, rigors, and pains in the limbs, followed by a purpuric eruption and general dropsy; the urine was albuminous, and contained epithelial casts and blood. Johnson believed that in this case, which terminated in recovery, the cutaneous eruption and the desquamative disease in the kidneys were primarily consequences of the poisoned state of the blood, and that the dropsy was a secondary result of the renal disease. A case analogous to Johnson's is reported by Girode.[37] Purpura hemorrhagica came on in the course of a chronic diffuse nephritis in an eight-year-old boy. The hemorrhages occurred very early in the disease, and suggested a common, infectious origin for both the purpura and the nephritis.

Samuel Gee[38] briefly mentions 3 interesting cases of purpura in children in association with nephritis. The onset was marked by diarrhœa, with blood in the stools; in 2 cases there was also vomiting. The purpura occurred in repeated accesses, but finally ceased, although the albuminuria persisted. These cases remind one of the erythema group so exhaustively described by Osler; in all probability they belong to it, and it is a fair assumption that the purpura, the diarrhœa, and the renal disturbances were all dependent upon one and the same infectious or toxic agent.

The history of the 2 cases that have come under my observation is as follows:

CASE I.—J. S., male, aged thirty years, a Russian tailor, was admitted to the Polyclinic Hospital on March 21, 1904, in the service of my colleague, Dr. Schneidemann, with a severe inflammation of the eye. The patient, whose faimily history was negative, had had no other illness, aside from measles in infancy, except two previous attacks of nephritis: the first seven years before, characterized by swelling of the feet, and, the second, two years later, in which the face was chiefly swollen. The third had begun three weeks before, with swelling of the face; but he was able to work until a few days prior to his entrance into the hospital. When admitted he was found to be pale and poorly nourished; the face was swollen, more particularly around the chin, the left eye, and the left malar and temporal regions. The left)eye was inflamed and reddened, and the conjunctiva chemotic. The right eye was painful on palpation, and its tension seemed increased. The heart was enlarged, the apex beat being in the sixth interspace in the nipple line; the first sound was muffled; the second much accentuated, with a tendency to reduplication; the radials and temporals were thickened. A blood examination showed: red blood corpuscles, 2,350,000; white blood corpuscles, 15,200; hemoglobin, 50 per cent., with a differential count as follows: polymorphonuclears, 78; small mononuclears, 13; large mononuclears, 4.5; eosinophiles, 3; transitionals, 1.5. There was no ascara; no ascites; no œdema of the legs; no enlargement of the spleen.

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[30] Loc. cit.

[31] Loc. cit.

[32] Manuel des maladies des reins et des capsules surrenales, 1906, 268.

[33] Practice of Medicine, sixth edition, 669 and 743.

[34] Quoted by Senator.

[35] Loc. cit.

[36] Diseases of the Kidneys, London, 1852, 152.

[37] Arch. de physiol. norm. et path., 1887, 3 s., ix, 478–485.

[38] St. Bartholomew's Hospital Reports, 1880, xvi, 47.

Dr. Schneidemann made a careful examination of the eye and reported as follows: "When the man came in he had redness and great œdema of both eyelids. Conjunctiva highly congested and chemotic; not tense, but relaxed and folded on itself. The lower conjunctiva was everted, and the upper slightly from the swelling; the motility of the eye was somewhat impaired, especially outward. The right pupil was moderately dilated, larger than the left, and immovable. Cornea was insensitive. Anterior chamber was extremely shallow. Iris nearly in contact with the cornea; tension + 2. A dull fundus reflex; but no details could be obtained. The œdema, mentioned above, extended to the region over the malar bone. On account of the man's condition, the functional testing of the eye for vision was unsatisfactory. There seemed to be some, but rather uncertain, perception for large objects. The patient complained of headache around the orbital, temporal, and malar regions."

On March 24 the patient began to bleed from the mouth, and, on examination, a carious tooth was found, which was thought to have caused a wound in the cheek; but, although the ragged edges of the tooth were broken off and styptic applications were made to the cheek, the bleeding continued. On account of the eye trouble, a leech was applied to the right temple; when it dropped off, there was free bleeding from the wound, a collodion dressing being required to check it.

On the 26th the patient had a convulsion, following which he was bled to the amount of fifteen ounces. After the venesection, he received an intravenous injection of 1200 c.c. of salt solution. Despite this, he had another convulsion on the same day.

On the 29th, a hemorrhagic suffusion appeared on the right side from the third rib to the costal margin, and a few purpuric spots were seen on the right arm. No history of an injury could be obtained, except the hypodermoclysis, which he had had three days before

On the same day he began to have hiccough, and gradually passed into a stuporous condition.

The ecchymosis on the right side became more extensive, and the spots on the right arm increased in number. Blood was running constantly from the mouth, and the breath was very fetid. The urine contained a large amount of albumin (1.5 parts in 1000), red blood corpuscles, and granular and hyaline casts.

On the 31st, a systolic murmur appeared, its area of maximum loudness in the third left interspace. Despite active treatment in the way of hot packs and stimulants, the pulse gradually grew weaker, and on April 1, eleven days after admission, the patient died. No autopsy could be obtained.

Case II.—W. D., tavernkeeper, aged fifty-five years, born in Philadelphia, was admitted to the Jewish Hospital, September 2, 1904. He had never been ill, and denied drinking to excess. He attributed his trouble, namely, hemorrhages from the mouth and bowels, which had begun eight weeks before, to having neglected his own health in attending to his wife while she was suffering from an attack of pneumonia. When admitted to the hospital he was stuporous and delirious, and in evident uremia. The breath was urinous, and, according to the history obtained, he had voided no urine for forty-eight hours. The mucous membranes were pale; the tongue and teeth covered with recent blood clots; the heart sounds clear; pulse slow and feeble; pupils widely dilated. There was no ascites; no enlargement of the abdominal veins. The urine, which had to be drawn, had a specific gravity of from 1010 to 1012; contained albumin, and red and white corpuscles. Blood examination showed: red corpuscles, 4,440,000; white corpuscles, 6680; hemoglobin, 55 per cent.; differential count: polymorphonuclears, 83 per cent.; lymphocytes, 9.6 per cent.; mononuclears, 4.7 per cent.; eosinophiles, 0.6 per cent.; transitionals, 2 per cent.

The man died in a convulsion on September 10, 1904; the bleeding having continued to the end. There were no purpuric spots upon the surface. The autopsy revealed marked anthracosis of the lungs; a moderately enlarged heart without valvular lesion, and a smooth liver of normal size. The kidneys were enlarged and covered with small cysts; the capsule stripped with difficulty. On section, the kidney showed an almost total absence of cortical substance and marked fibrosis; the cut surface bled freely. The pathologist thought that the condition was one of acute exacerbation of a chronic, diffuse nephritis. The gastrointestinal tract and urinary bladder were normal.

There are four ways in which one may interpret the relation of the hemorrhagic diathesis to renal disease:

1. The hemorrhagic diathesis may be an accident; that is, an independent affection not causally related to the nephritis. This would obtain in such cases in which a septic infection, as, for in-

stance, ulcerative endocarditis, coexisted with the renal disease and caused the hemorrhagic state.

2. The hemorrhagic diathesis may be the cause of the nephritis. Cases of this type, as has been previously stated, have been observed by Wagner and Senator. It might be difficult, however, to prove in a given instance that the third explanation does not better apply.

3. The two may be due to the same cause. This relation of the two conditions is fairly clear in a number of cases in the literature, notably those of Johnson, Gee, and Girode, already cited.

4. The renal disease may be the cause of the hemorrhagic diathesis. This is the explanation I would give for my own cases, and is the group to which I especially desire to call attention.

The question arises, in what particular way does the nephritis cause the hemorrhagic diathesis? Several possible etiological factors suggest themselves: (1) Hypertension; (2) arterial disease; and (3) toxemia.

The first and second are important factors in the ordinary types of nephritic hemorrhage. In all probability they are a sine qua non; but they are not of themselves sufficient to cause a true hemorrhagic diathesis, for the production of which another element, presumably a toxin, is necessary. Flexner's[39] studies on the effects of snake venom have shown the existence of substances, by him termed hemorrhagins, that are capable of causing hemorrhagic extravasations through a destructive action upon the capillary endothelium. Toxins with analogous properties may, as Fisher[40] has suggested, be present in the blood in nephritis. The hypothetic poison, whatever it may be, in addition to acting upon the vessel walls, may also impair the integrity of the blood—an impairment similar to that found in chronic jaundice.

Quite recently, Friedeman[41] found in the pancreatic juice a powerful hemolysin possessing the property of dissolving homologous red corpuscles and causing hemorrhages. In health it is neutralized by a protective substance; but we may conceive conditions—among them Bright's disease—in which this substance fails to act. In its power to cause hemorrhage and paralysis, the poison of the pancreas resembles crotalus venom.

Prognostically, nephritic hemorrhages of every variety constitute a sinister omen; the hemorrhagic diathesis in particular seems to presage an early death. It is evident that in every obscure case of hemorrhagic diathesis, as well as in cases of apparently causeless bleeding from mucous surfaces, the possibility of a renal origin should be borne in mind.

CONCLUSIONS. 1. Bright's disease may cause hemorrhage from the nose, uterus, lungs, and stomach; hemorrhage into the brain, eye, and ear; and also a more or less well-marked hemorrhagic diathesis.

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[39] Amer. Jour. Med. Sci., 1903, 202.

[40] Loc cit.

[41] Deutsche med. Wochenschr., 1907, Nr. 15.

2. The last-named condition is characterized by bleeding into the skin and from the mucous membranes.
3. The true cause of the hemorrhagic diathesis is unknown; but it is probably a toxin analogous to the hemorrhagins of snake venom.
4. In the other types of bleeding, arterial disease and hypertension are the chief factors.
5. The prognosis in all cases of nephritic hemorrhage is unfavorable, and generally hopeless when the hemorrhagic diathesis exists.

A CLINICAL STUDY OF FIVE HUNDRED CASES OF CONJUNCTIVITIS.[1]

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Conjunctivitis in its different forms constitutes one of the commonest diseases we have to deal with in ophthalmic practice. Its frequency varies according to race, climate, and environment; but when one considers how exposed the conjunctiva, a mucous membrane, is to external influences and how subject to involvement in nasal and postnasal inflammations, an average of 30 per cent. of all ophthalmic cases does not seem high. Conjunctivitis, too, more than any other disease of the eye, is treated by the general practitioner. In many cases he must treat it, so that I have thought it not out of place to report the results and lessons from a systematic examination of a series of cases.

In diseases of the eye, as in affections of other parts of the body, we look to etiology before prescribing or giving a prognosis. Our latest text-books still say: "As regards their etiology, much has yet to be learned, although considerable progress has been made in this direction within the past few years." It is quite true that much has yet to be learned, but enough is known today to enable us, by a bacteriological examination of the mucous or mucopurulent discharge, an important symptom of conjunctivitis, to obtain knowledge of much value in these directions. By using bacteriological methods we come to divide cases of conjunctivitis, not from their clinical features into catarrhal, purulent, and membranous with their numerous subdivisions, but rather into two groups: (1) Con-

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[1] Read at a meeting of the Montreal Medico-Chirurgical Society, June 7, 1907.